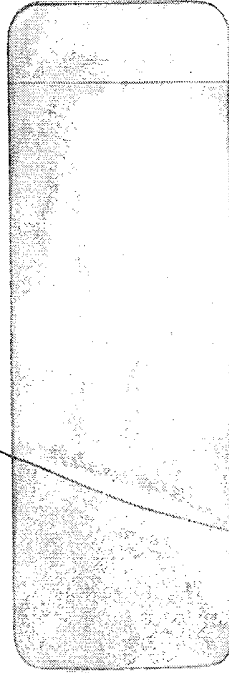
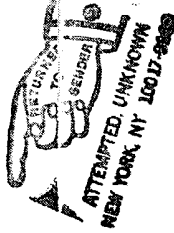


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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/764,970	01/18/2001	Edmund Bauerlein	0107-018A	8968

7590 03/08/2004

GABRIEL P. KATONA L.L.P.  
708 Third Avenue, 14th Floor  
New York, NY 10017

EXAMINER
----------

GIBBS, TERRA C

ART UNIT	PAPER NUMBER
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1635

DATE MAILED: 03/08/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

# Notice of Abandonment

Application No.

09/764,970

Examiner

Terra C. Gibbs

Applicant(s)

BAUERLEIN ET AL.

Art Unit

1635

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address--

This application is abandoned in view of:

1. ☒ Applicant's failure to timely file a proper reply to the Office letter mailed on 26 August 2003.
  - (a) ☐ A reply was received on \_\_\_\_\_ (with a Certificate of Mailing or Transmission dated \_\_\_\_\_), which is after the expiration of the period for reply (including a total extension of time of \_\_\_\_\_ month(s)) which expired on \_\_\_\_\_.
  - (b) ☐ A proposed reply was received on \_\_\_\_\_, but it does not constitute a proper reply under 37 CFR 1.113 (a) to the final rejection.  
(A proper reply under 37 CFR 1.113 to a final rejection consists only of: (1) a timely filed amendment which places the application in condition for allowance; (2) a timely filed Notice of Appeal (with appeal fee); or (3) a timely filed Request for Continued Examination (RCE) in compliance with 37 CFR 1.114).
  - (c) ☐ A reply was received on \_\_\_\_\_ but it does not constitute a proper reply, or a bona fide attempt at a proper reply, to the non-final rejection. See 37 CFR 1.85(a) and 1.111. (See explanation in box 7 below).
  - (d) ☒ No reply has been received.
2. ☐ Applicant's failure to timely pay the required issue fee and publication fee, if applicable, within the statutory period of three months from the mailing date of the Notice of Allowance (PTOL-85).
  - (a) ☐ The issue fee and publication fee, if applicable, was received on \_\_\_\_\_ (with a Certificate of Mailing or Transmission dated \_\_\_\_\_), which is after the expiration of the statutory period for payment of the issue fee (and publication fee) set in the Notice of Allowance (PTOL-85).
  - (b) ☐ The submitted fee of \$ \_\_\_\_\_ is insufficient. A balance of \$ \_\_\_\_\_ is due.  
The issue fee required by 37 CFR 1.18 is \$ \_\_\_\_\_. The publication fee, if required by 37 CFR 1.18(d), is \$ \_\_\_\_\_.
  - (c) ☐ The issue fee and publication fee, if applicable, has not been received.
3. ☐ Applicant's failure to timely file corrected drawings as required by, and within the three-month period set in, the Notice of Allowability (PTO-37).
  - (a) ☐ Proposed corrected drawings were received on \_\_\_\_\_ (with a Certificate of Mailing or Transmission dated \_\_\_\_\_), which is after the expiration of the period for reply.
  - (b) ☐ No corrected drawings have been received.
4. ☐ The letter of express abandonment which is signed by the attorney or agent of record, the assignee of the entire interest, or all of the applicants.
5. ☐ The letter of express abandonment which is signed by an attorney or agent (acting in a representative capacity under 37 CFR 1.34(a)) upon the filing of a continuing application.
6. ☐ The decision by the Board of Patent Appeals and Interference rendered on \_\_\_\_\_ and because the period for seeking court review of the decision has expired and there are no allowed claims.
7. ☒ The reason(s) below:

In a conversation with Cathy Barberry on March 2, 2004, the Examiner was informed that the Office Action, mailed August 26, 2003 was not received by Applicant, and therefore, no timely response was filed. The Examiner informed Ms. Barberry that the instant application would be abandoned and Applicant would have to file a petition under 37 CFR 1.137(a) to revive the instant application.

  
KAREN A. LACOURCIERE, PH.D.  
PRIMARY EXAMINER

Petitions to revive under 37 CFR 1.137(a) or (b), or requests to withdraw the holding of abandonment under 37 CFR 1.181, should be promptly filed to minimize any negative effects on patent term.

### Interview Summary

**Application No.**

09/764,970

**Applicant(s)**

BAUERLEIN ET AL.

**Examiner**

Terra C. Gibbs

**Art Unit**

1635

All participants (applicant, applicant's representative, PTO personnel):

(1) Terra C. Gibbs. (3)\_\_\_\_\_

(2) Cathy Barberry. (4)\_\_\_\_\_

Date of Interview: 02 March 2004.

Type: a) ☒ Telephonic b) ☐ Video Conference  
c) ☐ Personal [copy given to: 1) ☐ applicant 2) ☐ applicant's representative]

Exhibit shown or demonstration conducted: d) ☐ Yes e) ☐ No.  
If Yes, brief description: \_\_\_\_\_

Claim(s) discussed: \_\_\_\_\_


Identification of prior art discussed: \_\_\_\_\_

Agreement with respect to the claims f) ☐ was reached. g) ☐ was not reached. h) ☒ N/A.

Substance of Interview including description of the general nature of what was agreed to if an agreement was reached, or any other comments: See Continuation Sheet.

(A fuller description, if necessary, and a copy of the amendments which the examiner agreed would render the claims allowable, if available, must be attached. Also, where no copy of the amendments that would render the claims allowable is available, a summary thereof must be attached.)

THE FORMAL WRITTEN REPLY TO THE LAST OFFICE ACTION MUST INCLUDE THE SUBSTANCE OF THE INTERVIEW. (See MPEP Section 713.04). If a reply to the last Office action has already been filed, APPLICANT IS GIVEN ONE MONTH FROM THIS INTERVIEW DATE, OR THE MAILING DATE OF THIS INTERVIEW SUMMARY FORM, WHICHEVER IS LATER, TO FILE A STATEMENT OF THE SUBSTANCE OF THE INTERVIEW. See Summary of Record of Interview requirements on reverse side or on attached sheet.

  
KAREN A. LACOURCIERE, PH.D.  
PRIMARY EXAMINER

Examiner Note: You must sign this form unless it is an Attachment to a signed Office action.

\_\_\_\_\_  
Examiner's signature, if required

## Summary of Record of Interview Requirements

### Manual of Patent Examining Procedure (MPEP), Section 713.04, Substance of Interview Must be Made of Record

A complete written statement as to the substance of any face-to-face, video conference, or telephone interview with regard to an application must be made of record in the application whether or not an agreement with the examiner was reached at the interview.

### Title 37 Code of Federal Regulations (CFR) § 1.133 Interviews Paragraph (b)

In every instance where reconsideration is requested in view of an interview with an examiner, a complete written statement of the reasons presented at the interview as warranting favorable action must be filed by the applicant. An interview does not remove the necessity for reply to Office action as specified in §§ 1.111, 1.135. (35 U.S.C. 132)

#### 37 CFR §1.2 Business to be transacted in writing.

All business with the Patent or Trademark Office should be transacted in writing. The personal attendance of applicants or their attorneys or agents at the Patent and Trademark Office is unnecessary. The action of the Patent and Trademark Office will be based exclusively on the written record in the Office. No attention will be paid to any alleged oral promise, stipulation, or understanding in relation to which there is disagreement or doubt.

The action of the Patent and Trademark Office cannot be based exclusively on the written record in the Office if that record is itself incomplete through the failure to record the substance of interviews.

It is the responsibility of the applicant or the attorney or agent to make the substance of an interview of record in the application file, unless the examiner indicates he or she will do so. It is the examiner's responsibility to see that such a record is made and to correct material inaccuracies which bear directly on the question of patentability.

Examiners must complete an Interview Summary Form for each interview held where a matter of substance has been discussed during the interview by checking the appropriate boxes and filling in the blanks. Discussions regarding only procedural matters, directed solely to restriction requirements for which interview recordation is otherwise provided for in Section 812.01 of the Manual of Patent Examining Procedure, or pointing out typographical errors or unreadable script in Office actions or the like, are excluded from the interview recordation procedures below. Where the substance of an interview is completely recorded in an Examiners Amendment, no separate Interview Summary Record is required.

The Interview Summary Form shall be given an appropriate Paper No., placed in the right hand portion of the file, and listed on the "Contents" section of the file wrapper. In a personal interview, a duplicate of the Form is given to the applicant (or attorney or agent) at the conclusion of the interview. In the case of a telephone or video-conference interview, the copy is mailed to the applicant's correspondence address either with or prior to the next official communication. If additional correspondence from the examiner is not likely before an allowance or if other circumstances dictate, the Form should be mailed promptly after the interview rather than with the next official communication.

The Form provides for recordation of the following information:

- Application Number (Series Code and Serial Number)
- Name of applicant
- Name of examiner
- Date of interview
- Type of interview (telephonic, video-conference, or personal)
- Name of participant(s) (applicant, attorney or agent, examiner, other PTO personnel, etc.)
- An indication whether or not an exhibit was shown or a demonstration conducted
- An identification of the specific prior art discussed
- An indication whether an agreement was reached and if so, a description of the general nature of the agreement (may be by attachment of a copy of amendments or claims agreed as being allowable). Note: Agreement as to allowability is tentative and does not restrict further action by the examiner to the contrary.
- The signature of the examiner who conducted the interview (if Form is not an attachment to a signed Office action)

It is desirable that the examiner orally remind the applicant of his or her obligation to record the substance of the interview of each case. It should be noted, however, that the Interview Summary Form will not normally be considered a complete and proper recordation of the interview unless it includes, or is supplemented by the applicant or the examiner to include, all of the applicable items required below concerning the substance of the interview.

A complete and proper recordation of the substance of any interview should include at least the following applicable items:

- 1) A brief description of the nature of any exhibit shown or any demonstration conducted,
- 2) an identification of the claims discussed,
- 3) an identification of the specific prior art discussed,
- 4) an identification of the principal proposed amendments of a substantive nature discussed, unless these are already described on the Interview Summary Form completed by the Examiner,
- 5) a brief identification of the general thrust of the principal arguments presented to the examiner,  
(The identification of arguments need not be lengthy or elaborate. A verbatim or highly detailed description of the arguments is not required. The identification of the arguments is sufficient if the general nature or thrust of the principal arguments made to the examiner can be understood in the context of the application file. Of course, the applicant may desire to emphasize and fully describe those arguments which he or she feels were or might be persuasive to the examiner.)
- 6) a general indication of any other pertinent matters discussed, and
- 7) if appropriate, the general results or outcome of the interview unless already described in the Interview Summary Form completed by the examiner.

Examiners are expected to carefully review the applicant's record of the substance of an interview. If the record is not complete and accurate, the examiner will give the applicant an extendable one month time period to correct the record.

### Examiner to Check for Accuracy

If the claims are allowable for other reasons of record, the examiner should send a letter setting forth the examiner's version of the statement attributed to him or her. If the record is complete and accurate, the examiner should place the indication, "Interview Record OK" on the paper recording the substance of the interview along with the date and the examiner's initials.

Continuation of Substance of Interview including description of the general nature of what was agreed to if an agreement was reached, or any other comments: In a telephone conversation with Cathy Barberry, the Examiner was informed that the last Office Action, mailed August 26, 2003, was not received by Applicant. The Examiner informed Ms. Barberry that the instant application would be abandoned since no timely response was filed. Ms. Barberry informed the Examiner that she would file a petition under 37 CFR 1.137(a) to have the instant application revived. Additionally, Ms. Barberry requested that the Office Action that was mailed August 26, 2003 be sent to Applicant, so that their next response could include remarks regarding the previous Office Action .



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mailed 8/26/03

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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/764,970	01/18/2001	Edmund Bauerlein	0107-018A	8968

7590 08/26/2003

GABRIEL P. KATONA L.L.P.  
708 Third Avenue, 14th Floor  
New York, NY 10017

EXAMINER

GIBBS, TERRA C

ART UNIT	PAPER NUMBER
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1635

DATE MAILED: 08/26/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

**Office Action Summary**

Application No.

09/764,970

Applicant(s)

BAUERLEIN ET AL.

Examiner

Terra C. Gibbs

Art Unit

1635

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

- 1) ☐ Responsive to communication(s) filed on \_\_\_\_.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

- 4) ☒ Claim(s) 17, 18, and 19 is/are pending in the application.
- 4a) Of the above claim(s) 18 and 19 is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 17 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_ are subject to restriction and/or election requirement.

**Application Papers**

- 9) ☒ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
- Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- 11) ☐ The proposed drawing correction filed on \_\_\_\_ is: a) ☐ approved b) ☐ disapproved by the Examiner.
- If approved, corrected drawings are required in reply to this Office action.
- 12) ☒ The oath or declaration is objected to by the Examiner.

**Priority under 35 U.S.C. §§ 119 and 120**

- 13) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some \* c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- \* See the attached detailed Office action for a list of the certified copies not received.
- 14) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).
- a) ☐ The translation of the foreign language provisional application has been received.
- 15) ☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

**Attachment(s)**

- 1) ☒ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) \_\_\_\_.
- 4) ☐ Interview Summary (PTO-413) Paper No(s) \_\_\_\_.
- 5) ☐ Notice of Informal Patent Application (PTO-152)
- 6) ☐ Other: \_\_\_\_.



### DETAILED ACTION

Claims 17, 18, and 19 are pending in the instant application.

#### *Election/Restrictions*

Restriction to one of the following inventions is required under 35 U.S.C. 121:

- I. Claim 17, drawn to a magnetosome having a surface, and comprising a magnetite monocrystal having a diameter of at least 45 nm surrounded by a phospholipid membrane, and at least one therapeutic agent, classifiable in class 424, subclass 9.3.
- II. Claim 18, drawn to a process of treating a tumoral disease, inflammatory process, or metabolic disease, comprising the administration of a magnetosome having a surface, and comprising a magnetite monocrystal having a diameter of at least 45 nm surrounded by a phospholipid membrane, and at least one therapeutic agent, classifiable in class 514, subclass 2.
- III. Claim 19, drawn to a process for removing diseased cells, comprising the administration of a magnetosome having a surface, and comprising a magnetite monocrystal having a diameter of at least 45 nm surrounded by a phospholipid membrane, and at least one therapeutic agent, classifiable in class 435, subclass 69.1.

The inventions are distinct, each from the other because of the following reasons:

The composition invention of Group I is related to the method inventions of Groups II and III as product and process of use. The inventions can be shown to be distinct if either or

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both of the following can be shown: (1) the process for using the product as claimed can be practiced with another materially different product or (2) the product as claimed can be used in a materially different process of using that product (MPEP § 806.05(h)). In the instant case the products can be used in materially different processes of use. For example, the magnetosome having a surface, and comprising a magnetite monocrystal having a diameter of at least 45 nm surrounded by a phospholipid membrane, and at least one therapeutic agent of Group I can be used as a diagnostic agent for tumoral diseases, which is a materially different process than a method of treating a disease or a method of removing disease cells as in Groups II and III.

Inventions of Groups II and III are unrelated, each from the other. Inventions are unrelated if it can be shown that they are not disclosed as capable of use together and they have different modes of operation, different functions, or different effects (MPEP § 806.04, MPEP § 808.01). In the instant case, the different inventions are drawn to a method of treating a disease (Group I) and a method for removing diseased cells (Group II). In the instant case the different inventions are not disclosed as capable of use together and have different operations, functions, and effects. The two methods have different and noninterchangable steps that lead to different ends (e.g. methods of treatment vs. method of removing diseased cells). The methods of Group I can be used for therapeutic purposes while the methods of Group II can be used for diagnostic purging. The differences between Groups II and III are further underscored by their different classifications and independent search status. Thus, they are unrelated and patentably distinct from each other.

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Because these inventions are distinct for the reasons given above, restriction for examination purposes as indicated is proper.

During a telephone conversation with Attorney William Hwang on or around July 16, 2003, a provisional election was made with traverse to prosecute the invention of Group I, claim 17. Affirmation of this election must be made by applicant in replying to this Office action. Claims 18 and 19 are withdrawn from further consideration by the examiner, 37 CFR 1.142(b), as being drawn to a non-elected invention.

Applicant is advised that the reply to this requirement to be complete must include an election of the invention to be examined even though the requirement be traversed (37 CFR 1.143).

Applicant is reminded that upon the cancellation of claims to a non-elected invention, the inventorship must be amended in compliance with 37 CFR 1.48(b) if one or more of the currently named inventors is no longer an inventor of at least one claim remaining in the application. Any amendment of inventorship must be accompanied by a petition under 37 CFR 1.48(b) and by the fee required under 37 CFR 1.17(I).

Claim 17 is examined on the merits.

#### *Priority*

The reference to priority in the first line of the Specification should be updated with current serial numbers where patents have issued. Appropriate correction is required.

The instant application claims priority to USSN 09/397,705, filed 09/01/99, as a divisional. However, the instant application claims an invention not presented in the parent

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application (09/397,705) and further, appears to have a different disclosure than that of the parent application. For example, in comparing the Specification of the instant application with the Specification of the parent application, Table 2 of the instant application appears to be missing data that is present in the parent application (see Table 2, 110 h time point). Additionally, the instant application claims a magnetosome having a surface, and comprising a magnetite monocrystal having a diameter of at least 45 nm surrounded by a phospholipid membrane, and at least one therapeutic agent (see claim 17). The limitation of at least 45 nm is not found in the parent application. Accordingly, the instantly claimed invention has not been given priority back to the filing date of the parent application.

### *Specification*

The Specification is objected to because there is no Abstract. It is noted that Applicant provided an Abstract in the Amendment filed May 7, 2001 in Paper No. 5, however the Amendment was not entered because the Amendment was not submitted on a separate sheet of paper as required by amendment practice. See MPEP § 608.01(b). Correction is required.

Applicant is further reminded of the proper language and format for an abstract of the disclosure: The Abstract should be in narrative form and generally limited to a single paragraph on a separate sheet within the range of 50 to 150 words. It is important that the abstract not exceed 150 words in length since the space provided for the Abstract on the computer tape used by the printer is limited. The form and legal phraseology often used in patent claims, such as "means" and "said," should be avoided. The abstract should describe the disclosure sufficiently to assist readers in deciding whether there is a need for consulting the full patent text for details.

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The language should be clear and concise and should not repeat information given in the title. It should avoid using phrases which can be implied, such as, "**aforesaid**".

Further, Applicant should note, if the Abstract filed, May 7, 2001 is resubmitted in proper format, it may be entered, however, it may raise an issue under new matter (see 35 U.S.C. 112, first paragraph rejection against claim 17 as failing to comply with the written description requirement below).

#### ***Oath/Declaration***

The oath or declaration is defective. A new oath or declaration in compliance with 37 CFR 1.67(a) identifying this application by application number and filing date is required. See MPEP §§ 602.01 and 602.02.

The oath or declaration is defective because:

Non-initialed and/or non-dated alterations have been made to the oath or declaration. See 37 CFR 1.52(c).

#### ***Double Patenting***

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and, *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground

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provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claim 17 is rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claim 1 of U.S. Patent No. 6,251,365 ('365). Although the conflicting claims are not identical, they are not patentably distinct from each other because the magnetosome having a surface, and comprising a magnetite monocrystal having a maximum diameter of 45 nm surrounded by a phospholipid membrane of claim 1 of ('365) overlaps in scope with the magnetosome having a surface, and comprising a magnetite monocrystal having a diameter of at least 45 nm surrounded by a phospholipid membrane of the instant invention. The magnetosome having a diameter of at least 45 nm of the instant invention is an obvious species of the magnetosome having a maximum diameter of 45 nm of ('365). Therefore, a magnetosome having a diameter of exactly 45 nm of the patent would claim the same inventive concept of a magnetosome having a diameter of exactly 45 nm of the instant invention. A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or an amendment to the claims to exclude a magnetosome having a diameter of exactly 45 nm may be used to overcome this rejection.

***Claim Rejections - 35 USC § 112***

Claim 17 is rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described

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in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This is a new matter rejection.

Claim 17 is drawn to a magnetosome having a surface, and comprising a magnetite monocrystal having a diameter of "at least 45 nm" surrounded by a phospholipid membrane, and at least one therapeutic agent. There is no literal or inherent support in the instant Specification as filed for a magnetosome having a surface, and comprising a magnetite monocrystal having a diameter of at least 45 nm. Additionally, the parent application for which the instant application claims benefit contains no specific or inherent support for a magnetosome having a surface, and comprising a magnetite monocrystal having a diameter of "at least 45 nm" surrounded by a phospholipid membrane, and at least one therapeutic agent.

The specification, at page 1, lines 1-2, recites "The invention relates to specific magnetosomes with magnetic particles of maximally 43-45 nm". However, the Specification does not have support for "a magnetosome having a surface, and comprising a magnetite monocrystal having a diameter of at least 45 nm surrounded by a phospholipid membrane, and at least one therapeutic agent". Therefore, the limitation "at least 45 nm" (e.g. anything greater than 45 nm) is a new matter issue.

Applicant should specifically point out the support for any amendments made to the disclosure. See MPEP § 2163.06 which states, when filing an amendment, an applicant should show support in the original disclosure for new or amended claims (See MPEP § 714.02 and § 2163.06).

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It is noted that the Abstract filed, May 7, 2001 includes the limitation of "at least 45 nm", however, this Abstract was submitted post filing of the instant application and does not provide support at the date of filing of the instant application (01/18/01).

Applicant is required to cancel the new matter in the reply to this Office Action.

***Claim Rejections - 35 USC § 102***

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claim 17 is rejected under 35 U.S.C. 102(b) as being anticipated by Matsunaga et al. (Reprints from Ferrites: Proceedings of the Sixth International Conference on Ferrites, 1992).

Claim 17 is drawn to a magnetosome having a surface, and comprising a magnetite monocrystal having a diameter of at least 45 nm surrounded by a phospholipid membrane, and at least one therapeutic agent.

Matsunaga et al. disclose magnetic bacteria, AMB-1, containing magnetosomes, with an average particle size of 50-100 nm in diameter, covered with thin lipid films and immobilized enzymes, antibodies, or nucleic acids, can be utilized in biosensing systems with increased sensitivity (see page 262, first paragraph).

Therefore, Matsunaga et al. anticipate claim 17.



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Claim 17 is rejected under 35 U.S.C. 102(b) as being anticipated by Matsunaga et al. [U.S. Patent No. 6,033,878] ('878) as evidenced by Matsunaga et al. (Reprints from Ferrites: Proceedings of the Sixth International Conference on Ferrites, 1992).

Matsunaga et al. ('878) disclose isolated magnetic bacteria, AMB-1, which synthesized magnetic particles of magnetite of a very small size, which were enveloped by a membrane of phospholipids with chemically bound enzymes or antibodies (see Abstract, column 4, lines 4-16 and column 5, lines 12-24).

Matsunaga et al. ('878) do not explicitly state the diameter size of AMB-1, however AMB-1 has an average particle diameter of between 50 and 100 nm as evidenced by Matsunaga et al. (Reprints from Ferrites: Proceedings of the Sixth International Conference on Ferrites, 1992), see Introduction, for example. An average particle diameter of between 50 and 100 would be inherent to the AMB-1 of '878. This inherency is further evidenced by Applicants arguments filed in the parent application USSN 09/397,705, in Paper No. 13, filed October 16, 2000, where Applicants cited Matsunaga et al. (Reprints from Ferrites: Proceedings of the Sixth International Conference on Ferrites, 1992) as disclosing the size of AMB-1 particles by stating: "specifically identifies average particle diameters of magnetic particles AMB-1 and MGT-1 used by Matsunaga, specified as being between 50 and 100 nm, with the largest representing the mature crystal" (see forth paragraph, for example).

Therefore, Matsunaga et al. ('878) anticipate claim 17.

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*Conclusion*

No claims are allowable.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Terra C. Gibbs whose telephone number is (703) 306-3221. The examiner can normally be reached on M-F 8:30-5:00.

If attempts to reach the Examiner by telephone are unsuccessful, the examiner's supervisor, John L. LeGuyader can be reached on (703) 308-0447. The fax phone numbers for the organization where this application or proceeding is assigned are (703) 746-8693 for regular communications and (703) 872-9307 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.

tcg August 19, 2003

  
KAREN LACOURCIERE  
PATENT EXAMINER

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<b>Notice of References Cited</b>	Application/Control No. 09/764,970	Applicant(s)/Patent Under Reexamination BAUERLEIN ET AL.	
	Examiner Terra C. Gibbs	Art Unit 1635	Page 1 of 1

**U.S. PATENT DOCUMENTS**

*		Document Number Country Code-Number-Kind Code	Date MM-YYYY	Name	Classification
	A	US-6,033,878	03-2000	Matsunaga, Tadashi	435/69.7
	B	US-			
	C	US-			
	D	US-			
	E	US-			
	F	US-			
	G	US-			
	H	US-			
	I	US-			
	J	US-			
	K	US-			
	L	US-			
	M	US-			

**FOREIGN PATENT DOCUMENTS**

*		Document Number Country Code-Number-Kind Code	Date MM-YYYY	Country	Name	Classification
	N					
	O					
	P					
	Q					
	R					
	S					
	T					

**NON-PATENT DOCUMENTS**

*		Include as applicable: Author, Title Date, Publisher, Edition or Volume, Pertinent Pages)
	U	Matsunaga et al. Production of biogenic magnetite by aerobic magnetic spirilla strains AMB-1 and MGT-1. Reprints from Ferrites: Proceedings of the Sixth International Conference on Ferrites, 1992.
	V	
	W	
	X	

\*A copy of this reference is not being furnished with this Office action. (See MPEP § 707.05(a).)  
Dates in MM-YYYY format are publication dates. Classifications may be US or foreign.

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## PRODUCTION OF BIOGENIC MAGNETITE BY AEROBIC MAGNETIC SPIRILLA STRAINS AMB-1 AND MGT-1

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**Abstract** Two strains of magnetic spirilla were obtained as pure cultures from two separate freshwater sediment samples. Under microaerobic conditions both spirilla produced 2.3–2.6 mg of biogenic magnetite ( $\text{Fe}_3\text{O}_4$ ) per liter of culture and possessed oxygen tolerance. In addition, taxonomic characteristics of these strains were investigated. They were found to be morphologically similar, however carbon source utilization differences suggested that they are two independent strains.

**KEY WORDS:** MAGNETIC BACTERIA, MAGNETITE, PURE CULTIVATION, BACTERIAL GROWTH, SEDIMENT

### I. INTRODUCTION

Magnetic bacteria of diverse morphologies have been found in freshwater, marine sediment [1], and soil [2]. These bacteria contain magnetosomes which consist of 10–30 magnetic particles aligned in a chain or arranged randomly. These ultrafine magnetic particles are covered with thin lipid films [3]. The average of the particles of diameter is 50–100 nm. In most cases, the magnetic particles are composed of magnetite ( $\text{Fe}_3\text{O}_4$ ) with single domain. We have carried out biotechnological application of magnetic bacteria and their magnetic particles. We have immobilized enzymes, antibodies, or nucleic acids onto these particles and used them for producing biosensing systems with increased sensitivity [3–7]. Recently, we also developed a method for the detection and recovery of specific DNA or RNA using DNA immobilized on biogenic magnetite from magnetic bacteria [8]. For these applications, the availability of biogenic magnetite from magnetic bacteria has been shown.

For practical application of biogenic magnetite, mass cultivation of magnetic bacteria is required. However, it is difficult to cultivate magnetic bacteria, and only five pure cultures (including AMB-1 and MGT-1) have been obtained since their discovery in 1975 [9,10,11,12,13]. The first magnetic bacterium to be isolated; *Magnetospirillum* (*Aquaspirillum*) *magnetotacticum* strain MS-1, the most thoroughly studied magnetic bacterium is an obligate microaerophile [10]. Magnetic bacteria in natural environments have thus been considered to have similar characteristics with this strain. On the other hand, we have attempted to isolate magnetic bacteria from the natural environment, and have obtained two strains of magnetic spirilla from freshwater (AMB-1 and MGT-1) which are capable of growing in an air atmosphere

[12,13]. Recently, we have established a gene transfer system in the magnetic bacterium. We have obtained five transposon Tn 5 non-magnetic mutants. Two genomic fragments containing mutagenized regions have been cloned into *E. coli* [14].

We report here the properties of two aerobic magnetic spirilla strains AMB-1 and MGT-1, characterization of their intracellular magnetic particles, for the production of biogenic magnetite for biotechnological application.

### II. MATERIALS AND METHODS

#### Isolation and Purification of Magnetic Bacteria

The procedure for isolation of magnetic bacteria from natural sediment has been described previously [13]. Bacteria were magnetically purified with a samarium-cobalt magnet (produced by TDK, Tokyo, Japan) and a capillary glass isolation apparatus plugged with cotton. After colony formation, the isolated magnetic bacteria were spread on 0.7% agar plates of chemically defined medium [10], and were isolated as pure cultures (designated AMB-1 and MGT-1) by picking up single colonies from the plates and restreaking several times.

#### Observation of Isolated Magnetic Bacteria by Light and Electron Microscopy

Isolated and purified magnetic bacteria were observed by phase contrast microscopy (Model 2PC OLYMPUS Co Japan). Their morphology, shape, size and motility were recorded. These bacteria were negatively stained with 1% phosphotungstic acid (pH 6.2), and observed with a transmission electron microscope (TEM).

#### Cultivation of Magnetic Bacteria under Aerobic and Microaerobic Conditions

in the presence of  $\text{SnCl}_4$  catalyst. The nonseparable fraction, recovered by steam distn., is hydrogenated and purified by sapon. with methanolic KOH, distn. in vacuum, decolorization, and deparaffination, to give squalane. Olive oil refining byproducts (10,000 kg) were esterified at  $250^\circ$  in vacuum, with 1,620 kg trimethylolpropane, in the presence of 0.01%  $\text{SnCl}_4$ . The product was subjected to steam distn. and the distillate was hydrogenated in the presence of Raney Ni. The product (2,000 kg) was sapon. with 140 kg KOH in 60 kg  $\text{H}_2\text{O}$  and 170 kg MeOH, at  $100^\circ$ , followed by distn. at 4 mm Hg pressure. The distillate was decolorized with charcoal at  $85^\circ$ , with subsequent filtration, cooling of the filtrate to  $5^\circ$  and a 2nd filtration to give squalane of 97.4% purity.

109: 176327v Nonsaponifiable soybean oil fraction as an hypolipemic drug. Antibioticos S. A. Spain, ES 481,093 (Cl. A61K31/20), 01 Nov 1980, Appl. 30 May 1979; 64 pp. The title fraction comprises 40-50% vegetable sterols and 18-22% tocopherols, the balance being fundamental fatty acids. The fraction is prep'd. by steam distn. of soybean oil, to give an odor-free distillate contg. 25-30% vegetable sterols and 14-18 tocopherols. The distillate is treated with MeOH, in order to convert the fatty acids into Me esters, which are removed by mol. distn. at  $170-190^\circ$  and 20-130 Hg pressure. The residue is the hypolipemic drug. Daily administration of the encapsulated drug, for 9 days, decreased the blood cholesterol level by 57% in hypercholesterolemic patients. A mixt. of soybean oil nonsaponifiable fraction 470, vitamin C 20, citric acid 10, cellulose glycolate 40, Na laurylsulfate 20 and ethoxylated stearate 10 g was treated with 800 mL halohydrin solvent and 390 g Aerosil 200-400, followed by heating to  $50-60^\circ$  and pulverization. The powder was granulated with a soln. of 40 g PVP in EtOH-chloroethane mixt., to give a drug.

109: 176328w Process for the extraction of quinine from cinchona bark by supercritical carbon dioxide. Mueller, Adam Ger. Offen. DE 2,704,850 (Cl. C07D463/04), 25 Aug 1988, Appl. 16 Feb 1987; 3 pp. A process and app. for the extn. of quinine from cinchona bark by supercrit.  $\text{CO}_2$  are described.

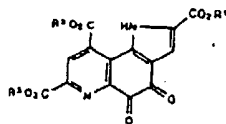
109: 176329x Liposomes containing magnetite. Gomiya, Hideyuki Kaneki, Hiroyuki (Shiseido Co., Ltd.) Jpn. Kokai Tokkyo Koho JP 63 14,717 (Cl. A61K9/10), 21 Jan 1988, Appl. 86/159,447, 07 Jul 1988; 5 pp. Liposomes comprising chemothapeutic agents and magnetite are useful as a drug targeting device. Magnetite was prep'd. from *Spirillum volutans* by treating the organisms with 0.2% lysozyme for 1 h at  $37^\circ$  and followed by 6M NaOH for 12 h. Phospholipid membranes contg. actinomycin D 300  $\mu\text{g}$ , dipalmitoylphosphatidylcholine 0.1 g and cetyl phosphate 4 mg were stirred with the above magnetite at 0.1% by wt. to give liposomes. The liposome (50  $\mu\text{L}$ ) was i.v. administered to mice bearing Ehrlich carcinoma and the survival rate was obs'd.; the liposome contg. 1.0  $\mu\text{g/mL}$  of actinomycin D prolonged the survival days to  $\geq 100$  days, whereas control mice survived on the av. 20.5 days.

109: 176320r Preparation of chitosan particles by spray-drying of acidic chitosan solution. Sugaya, Toshiko; Murakami, Hiroko; Katayama, Hirokazu (Dainichiseika Color and Chemicals Mfg. Co., Ltd.) Jpn. Kokai Tokkyo Koho JP 83 20,302 (83 20,302) (Cl. C08B37/08), 29 Jan 1988, Appl. 86/162,083, 11 Jul 1988; 4 pp. Chitosan particles are prep'd. by spray-drying of acidic chitosan soln. AcOH (mol. wt. 23  $\times 10^4$ ) deacetylated 63% was dissolved in 1% pressure at a flow rate of 5-6 mL/min and  $130^\circ$ . The particles were found spherical, and the av. diam. 2  $\mu\text{m}$ .

109: 176331s Preparation of minute particles of chitosan. Sugaya, Toshiko; Murakami, Hiroko; Katayama, Hirokazu (Dainichiseika Color and Chemicals Mfg. Co., Ltd.) Jpn. Kokai Tokkyo Koho JP 83 20,301 (83 20,301) (Cl. C08B37/08), 29 Jan 1988, Appl. 86/162,087, 11 Jul 1988; 4 pp. Chitosan microparticles with av. diam.  $\leq 10 \mu\text{m}$  are prep'd. Chitosan (mol. wt. 23  $\times 10^4$ ) 63% deacetylated was dissolved in 1% AcOH to make a 0.1% soln. This soln. was spray-dried under 1 kg/cm<sup>2</sup> pressure at a rate of 3-6 mL/min and  $130^\circ$ . The av. particle diam. was 2  $\mu\text{m}$ .

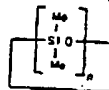
109: 176332t Preparation of chitosan powder for pharmaceuticals. Yamanami, Takao; Tsuchida, Shinya; Seki, Mitsunaka (Dainichiseika Color and Chemicals Mfg. Co., Ltd.) Jpn. Kokai Tokkyo Koho JP 63 17,902 (83 17,902) (Cl. C08B37/08), 25 Jan 1988, Appl. 86/160,930, 10 Jul 1988; 4 pp. Chitosan powder is prep'd. by spray-drying chitosan acid soln. in an  $\text{NH}_3$  atm. Chitosan (mol. wt. 23  $\times 10^4$ ) 63% deacetylated was dissolved in 1% AcOH to make a 0.1% soln., and this soln. was spray-dried in an atm. contg. 1000 ppm  $\text{NH}_3$  at 1-2 mL/min under 1 kg/cm<sup>2</sup> pressure at the introduction temp. of  $50^\circ$ . The powder obtained was dispersed in EtOH, isolated by centrifugation, and dried to give a chitosan powder. The particles were spherical and had an av. diam. of 2  $\mu\text{m}$ . Chitosan had immunostimulating activity and may be i.v. injected into patients.

109: 176333u pyrroloquinoline quinone derivatives as reverse transcriptase inhibitors. Katsumata, Manabu; Osawa, Yasuko; Nakagiri, Tomoo; Uchikawa, Saburo (Sogo Yakuko Co., Ltd.) Jpn. Kokai Tokkyo Koho JP 63,156,724 (83,156,724) (Cl. A61K31/47), 29 Jun 1988, Appl. 86/301,388, 18 Dec 1986; 4 pp. Reverse



transcriptase inhibitors, which are useful for prophylactic and therapeutic treatment of diseases caused by retrovirus, contain the title comp'd. I ( $\text{R}_1-\text{R}_4 = \text{H}$ , alkyl, alkyl metal, 1/2 alk. earth metal) as active ingredients. I ( $\text{R}_1-\text{R}_4 = \text{H}$ ) (II) di-K salt, II di-Me Et ester, and II tri-Me ester exhibited  $\text{IC}_{50}$  values of  $2.2 \times 10^{-4}$ ,  $7.3 \times 10^{-4}$ , and  $5.3 \times 10^{-4}$  M in reverse transcriptase in porcine leukemia 90, corn starch 29, and Mg stearate 1 part by wt.

109: 176334v cyclic dimethyl polysiloxane-containing gel compositions for cosmetic and pharmaceutical pastes and creams. Mori, Shigeru; Kuwata, Satoshi (Shin-Etsu Chemical Industry Co., Ltd.) Jpn. Kokai Tokkyo Koho JP 63,159,459 (83,159,459) (Cl. C09K3/00), 02 Jul 1988, Appl. 86/310,534, 23 Dec 1986; 4 pp. Gel compns. contain cyclic di-Me polysiloxane (I; n



$n = 4, 5$ , or 6; d. p. 4-6) 90-30, animal or vegetable oils and/or vaseline 5-50, and dextrin fatty acid esters 5-30 parts. The compns. are applied smoothly to the skin and are not tacky. KF 995 (decamethyl cyclotetrasiloxane) 70, jojoba oil 15, and Rheopariol KL (dextrin fatty acid ester) 15 parts were mixed at  $60-70^\circ$  and quickly cooled to give a gel compn. suitable for pharmaceutical and cosmetic preps., having the consistency value of 261 and the extant of oil release of 0.7% at  $40^\circ$  in 24 h; the gelation did not occur in the absence of jojoba oil.

109: 176325w Pharmaceutical products containing calcium mixed salts of polymeric, anionic hydroxy carboxylic acids and/or their sulfate esters for treatment of hyperphosphatemia and prevention of phosphate- and oxalate-containing kidney stones formation. Kulbe, Klaus D.; Weber, Hans (Algina A.-G.) U.S. US 4,689,322 (Cl. 514-54; A61K31/716), 25 Aug 1987, DE Appl. 3,228,321, 28 Jul 1982; 16 pp. Cont-in-part of U.S. Ser. No. 516,787, abandoned. The title oral pharmaceutical, useful for chronic uremia and/or the control of oxalate and/or phosphate of the blood in kidney stone prophylaxis, comprises a salt of a natural polymeric anionic carboxylic acid (cation = Ca or Ca + Fe or trace element) with the total cation in salt being present at 0.5-5.0 times the stoichiometric amt. and the Ca and other cation being present at 0.46-4.95 and 0.05-2.5 times the stoichiometric amt., resp. together with a pharmaceutical carrier in the form of beads, capsules, tablets, powders, dragees, or pills. Kelp alginate acid (8 g) was dissolved in 80 mL  $\text{H}_2\text{O}$  under stirring, the pH was adjusted to 7.4 (1M NaOH), and stirred for 2 h at room temp. and then left for 12 h. This Na alginate soln. was added dropwise into a 0.4M  $\text{CaCl}_2$  soln. forming beads having a dia.  $\sim 5$  mm; these beads were fully hard in 12 h at  $4^\circ$ . Ca salts not bound were removed by washing the beads with 3 times the vol. of water. Ca/Fe mixed salts were prep'd. by using an induration soln. (500 mL) contg. 0.25M  $\text{FeCl}_3$  and 0.4M  $\text{CaCl}_2$ . The in vitro phosphate-binding capacity, per g. of a binder was 0.34 g  $\text{PO}_4^{3-}$  for Ca alginate compared with 0.17 g for Aldurox  $[\text{Al}(\text{OH})_3]$ . Patients with chronic kidney failure, which had been given hemodialysis treatment, and which despite conventional therapy with  $\text{Al}(\text{OH})_3$  were showing an excessive level of serum-phosphate, were treated with 5.4 g Ca alginate/day and after 6 mo the serum-phosphate levels were reduced from 8.5 mg% to 6.1 mg% which is an acceptable level. While  $\text{K}^+$  values did not change, a lower retn. of Ca levels was measured; side reaction were not obs'd. There was a noticeable lowering of the constipation assoc. with the  $\text{Al}(\text{OH})_3$  therapy.

109: 176338x Transdermal compositions containing urea. Nakagawa, Akira; Miyata, Satoru; Kasai, Hiroaki (Hisamitsu Pharmaceutical Co., Inc.) Jpn. Kokai Tokkyo Koho JP 62,223,163 (87,223,163) (Cl. C07C126/08), 01 Oct 1987, Appl. 86/55,816, 12 Mar 1988; 6 pp. The compn. comprises urea, hydrocarbon, higher alc., and nonionic surfactants. A formulation contained petrolatum 15, cetostearyl alc. 10, paraffin oil 5, polyoxyethylene cetyl ether 3, methylparaben 0.2 g and urea (5 g; dissolved in  $\text{H}_2\text{O}$ ). This formulation was kept at  $40^\circ$ . After 20 days at this temp., the percentage of unchanged urea was 99.5%, vs. 34.9% for a com. formulation.

109: 176337y Amines as transdermal drug absorption promoters. Kamiya, Tetsuro; Matsuo, Noboru; Monaka, Tomonori; Hara, Kenji (Kao Corp.) Jpn. Kokai Tokkyo Koho JP 62,240,628 (87,240,628) (Cl. A61K47/00), 21 Oct 1987, Appl. 86/67,874, 28 Mar 1988; 7 pp. Transdermal compns. contain amines  $\text{NR}_1\text{R}_2\text{R}_3$  (I;  $\text{R}_1 = \text{R}_2 = \text{C}$ -as said, or unsatd. aliph. (alicyclic) hydrocarb.,  $\text{C}$ -alkylphenyl) as drug absorption promoters. A compn. contg. iteban 97 and dimethylstearylamine 3 g was prep'd. (Itaban is an indomethacin ointment prep'd. by Sumitomo Chem. Co. Ltd.). After a sample of this compn. contg. 20 mg indomethacin was applied to rabbit skin, the peak blood level of indomethacin was 920 ng/mL, vs. a level of 72 ng/mL for iteban.

109: 176338z Pharmaceuticals containing (+)-(2S,3S)-3-(S)-o-3-methyl-1-(3-methylbutylcarbamoyl)borhyloarhamoyl-2-oxi-ranecarboxylic acid for treatment of acute central nervous system disorders. Iwasaki, Yuzo (Taisho Pharmaceutical Co., Ltd.) Jpn. Kokai Tokkyo Koho JP 62,255,423 (87,255,423) (Cl. A61K31/336), 07 Nov 1987, Appl. 86/97,342, 26 Apr 1986; 6 pp. The title comp'd. (I), its salts or alkyl esters are pharmaceuticals for treatment of acute central nervous system disorders. I Et ester 100, corn starch 50, and cryst. cellulose 50 g were mixed, pulverized,